

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Sasisekharan, et al.  
Serial No: 09/384,959  
Filed: August 27, 1999  
For: RATIONALLY DESIGNED HEPARINASES DERIVED  
FROM HEPARINASE I AND II  
Examiner: Unassigned  
Art Unit: 1643

## CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231, on the 17th day of February, 2000.

Kim Ray Akeeli

THE ASSISTANT COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231

Sir:

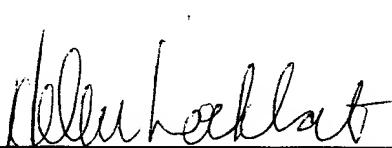
Transmitted herewith are the following documents:

- Information Disclosure Statement
- Form 1449 and References Cited
- Return Receipt Postcard

If the enclosed papers are considered incomplete, the U.S. Patent and Trademark Office is respectfully requested to contact the undersigned at (617)720-3500, Boston, Massachusetts.

If any fee is required, please charge to the account of the undersigned, Deposit Account No. 23/2825. A duplicate of this sheet is enclosed.

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By: 

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TC 160C  
FEE  
RE

Docket No. M0656/7046  
Dated: February 17, 2000  
NDD

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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**CERTIFICATE OF MAILING UNDER 37 CFR §1.8(e)**

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Kim Ray Deen

Assistant Commissioner for Patents  
Washington, D.C. 20231

**STATEMENT FILED PURSUANT TO THE DUTY OF  
DISCLOSURE UNDER 37 CFR §§1.56, 1.97 AND 1.98**

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, the Applicants request consideration of this Information Disclosure Statement.

**Compliance with 37 C.F.R. §1.97**

This Information Disclosure Statement has been filed before the filing date of a first office action, therefore there is no fee due.

**Information Cited**

The Applicants hereby make of record in the above-identified application the information listed on the attached form PTO-1449 (modified). The order of presentation of the references should not be construed as an indication of the importance of the references.

**Other Information**

The Applicants hereby make the following additional information of record in the above-identified application:

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The following is a related pending U.S. non-provisional applications which does not appear on the 1449 form.

<u>Serial No.</u>	<u>Filing Date</u>
09/066,481	October 30, 1996

Remarks

A copy of each of the above-identified information is enclosed unless otherwise indicated on the attached form PTO-1449 (modified). It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;
2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application;
3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the Applicants make no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

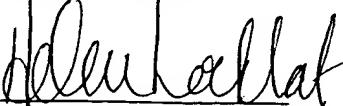
By submitting this Information Disclosure Statement, the Applicants make no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b).

By submitting this Information Disclosure Statement, the Applicants make no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

Notwithstanding any statements by the Applicants, the Examiner is urged to form his own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

Respectfully submitted,

By:   
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Tel. (617)720-3500

Docket No. M0656/7046  
Dated: February 17, 2000

LIST OF PATENTS AND PUBLICATIONS FOR A PATENT INFORMATION DISCLOSURE STATEMENT

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SASISEKHARAN, et al.

FILING DATE: August 27, 1999

GROUP: 1643

## U.S. PATENT DOCUMENTS

Exam Init	Ref Des	Document No.	Date	Name	Class	Sub Class	FILING DATE If Appropriate
	A1	4,281,108	07/28/81	Fussi	536	21	
	A2	4,745,105	05/17/88	Griffin et al.	514	56	
	A3	4,757,056	07/12/88	Van Gorp et al.	514	54	
	A4	4,942,156	07/17/90	Foley et al.	514	56	
	A5	4,990,502	02/05/91	Lormeau et al.	514	56	
	A6	5,010,063	04/23/91	Piani et al.	514	56	
	A7	5,039,529	08/13/91	Bergendal et al.	424	630	
	A8	5,106,734	04/21/92	Nielsen	435	84	
	A9	5,152,784	10/06/92	Tsilibary	623	1	
	A10	5,169,772	12/08/92	Zimmerman et al.	435	232	
	A11	5,204,323	04/20/93	Findlay et al.	514	2	
	A12	5,252,339	10/12/93	Cristofori et al.	424	479	
	A13	5,262,325	11/16/93	Zimmermann et al.	435	269	
	A14	5,290,695	03/01/94	Morikawa et al.	435	232	
	A15	5,338,677	08/16/94	Zimmermann et al.	435	200	
	A16	5,474,987	12/12/95	Cohen et al.	514	56	
	A17	5,576,304	11/19/96	Kakkar et al.	514	56	
	A18	5,599,801	02/04/97	Branellec et al.	514	56	
	A19	5,618,917	04/08/97	Toback et al.	530	350	
	A20	5,681,733	10/28/97	Su et al.	435	232	
	A21	5,744,515	04/28/98	Clapper	523	113	
	A22	5,753,445	05/19/98	Fillit et al.	435	7.1	
	A23	5,763,427	06/09/98	Weitz et al.	514	56	
	A24	5,922,358	07/13/99	Doutremepuich et al.	424	553	
	A25	5,795,875	08/18/98	Holme et al.	514	56	
	A26	5,808,021	09/15/98	Holme et al.	536	21	
	A27	5,824,299	10/20/98	Luster et al.	424	85.1	
	A28	5,919,693	07/06/99	Su et al.	435	252.3	
	A29	5,997,863	12/07/99	Zimmermann et al.	424	94.5	
	A30	6,013,628	01/11/00	Skubitz et al.	513	12	
	A31	5,164,378	11/17/92	Conti, et al.	514	56	
	A32	5,830,726	11/3/98	Sasisekharan et al.	435	172.3	
	A33	5,714,376	2/3/98	Sasisekharan et al.	435	252.3	
	A34	5,619,421	4/8/97	Venkataraman et al.	346	496	
	A35	5,569,600	10/29/96	Sasisekharan et al.	435	220	
	A36	5,567,417	10/22/96	Sasisekharan et al.	424	94.5	
	A37	5,389,539	2/14/95	Sasisekharan et al.	435	220	
	A38	4,443,545	4/17/84	Langer, Jr. et al.	435	232	
	A39	4,396,762	8/2/83	Langer, et al.	536	21	
	A40	4,373,023	2/8/83	Langer, et al.	435	2	
	A41	4,341,869	7/27/82	Langer, Jr. et al.	435	232	

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		Country & Doc. No. (11)	Pub. Date (43)		Class	Sub Class	Translation Yes No
	<b>B1</b>	EP 0 433 225 A1	11/27/90	Ciba-Geigy AG			
	<b>B2</b>	EP 0 557 887 A2	02/18/93	Opocrin S.p.A.			
	<b>B3</b>	WO 93/19096	09/30/93	Cancer Research Campaign Techn., Ltd.			
	<b>B4</b>	WO 94/21689	09/29/94	Cancer Research Campaign Techn., Ltd.			
	<b>B5</b>	WO 97/16556	05/09/97	Massachusetts Institute of Technology			
	<b>B6</b>	PCT/US96/17310	10/30/96	PCT Search Report			
	<b>B7</b>	WO93/08289	04/29/93	Massachusetts Institute of Technology			

**OTHER ART**  
(Including Author, Title, Date, Pertinent Pages, Publication, Etc.)

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C1		Karen A. Valentine, M.D. et al., "Low-Molecular-Weight Heparin Therapy and Mortality," <i>Seminars in Thrombosis and Hemostasis</i> , Vol. 23, No. 2, 1997, pp. 173-178
C2		Robert J. Linhardt, Ph.D. et al., "Production and Chemical Processing of Low Molecular Weight Heparins," <i>Seminars in Thrombosis and Hemostasis</i> , Vol. 25, Suppl. 3, 1999, pp. 5-16
C3		James N. Huang, MD. et al., "Low-Molecular-Weight Heparins", <i>Coagulation Disorders</i> , Vol. 12, No. 6, December 1998, pp. 1251-1277
C4		Richard L. Jackson et al., "Glycosaminoglycans: Molecular Properties, Protein Interactions, and Role in Physiological Processes", <i>Reviews</i> , Vol. 71, No. 2, April , 1991, pp. 481-539
C5		Gerald W. Hart, "Glycosylation", <i>Current Opinion in Cell Biology</i> , 1992, 4:1017-1023
C6		Pita Enriquez-Harris et al., "Growth Factors and the Extracellular Matrix", <i>Meeting Report, Trends in Cell Biology</i> , 1994
C7		Fred E. Cohen, "The Parallel $\beta$ Helix of Pectate Lyase C: Something to Sneeze At, <i>Science</i> , Vol. 260, June 4, 1993, pp. 1444-1445
C8		Ulrich Baumann et al., "Three-dimensional structure of the alkaline protease of <i>Pseudomonas aeruginosa</i> : a calcium binding parallel beta roll motif", <i>The EMBO Journal</i> , vol. 12, no. 9, pp. 3357-3364, 1993
C9		Marilyn D. Yoder et al., "Unusual structural features in the parallel $\beta$ -helix in pectate lyases", <i>Structure</i> , December 15, 1993, 1:241-251
C10		Marilyn D. Yoder et al., "New Domain Motif: The Structure of Pectate Lyase C., a Secreted Plant Virulence Factor", <i>Science</i> , Vol 260, June 4, 1993, pp. 1503-1506
C11		Michael J. Franklin et al, "Pseudomonas aeruginosa AlgG is a Polymer Level Alginate C5-Mannuronan Epimerase", <i>Journal of Bacteriology</i> , Vol. 176, No. 7, April 1994, p. 1821-1830
C12		David Sidney Feingold et al., "Conformational aspects of the reaction mechanisms of polysaccharide lyases and epimerases", <i>FEBS Letters</i> , Vol. 223, No. 2, November, 1987, pp. 207-211
C13		Peter Gacesa, "Alginate-modifying enzymes - A proposed unified mechanism of action for the lyases and epimerases", <i>FEBS LETTERS</i> , Vol. 212, No. 2, February, 1987, pp. 199-202
C14		Florentyna Lustig et al., "Alternative Splicing Determines the Binding of Platelet-Derived Growth Factor (PDGF-AA) to Glycosaminoglycans", <i>Biochemistry</i> , vol. 35, No. 37 1996, pp. 12077-12085.
C15		Ranga Godavarti et al., "Heparinase I from <i>Flavobacterium heparinum</i> . Identification of a Critical Histidine Residue Essential for Catalysis As Probed by Chemical Modification and Site-Directed Mutagenesis" <i>Biochemistry</i> , 1996, 35, 6846-6852
C16		Ram Sasisekharan et al., "Heparinase I from <i>Falbocacterium heparinum</i> ", <i>The Journal of Biological Chemistry</i> , Vol. 271 No. 6, Issue February 9, pp. 3124-3131
C17		Ram Sasisekharan et al., "Heparinase I from <i>Flavobacterium heparinum</i> " The Role of the Cysteine Residue in Catalysis as Probed by Chemical Modification and Site-Directed Mutagenesis", <i>Biochemistry</i> , Vol. 34, No. 44, 1995, pp. 14441-14448

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	C18	Lewin, B., et al., "Obey the Laws of Physics & Chemistry", <i>GENES V</i> , 1994, p.13
	C19	Bernstein, H., et al., <i>Methods in Enzymology</i> , (1988), 137:515-529
	C20	Cardin, A., et al., <i>Arteriosclerosis</i> , (1989), 9:21-32
	C21	Comfort, A., et al., <i>Biotech and Bioeng.</i> , (1989), 34:1383-1390,
	C22	Higuchi, R., et al., "PCR Protocols: A Guide to Methods and Applications", <i>Academic Press, Inc.</i> NY, (1990), 177-183
	C24	Kretsinger, R., et al., <i>CRC Crit., Rev. Biochem.</i> , (1980), 8:119-174
	C25	Leckband, D., et al., <i>Biotech Bioeng.</i> , (1991), 37:227-237
	C26	Linhardt, R., et al., <i>Appl. Biochem. Biotechnol.</i> (1986), 12:135-176
	C27	Linhardt, R., et al., <i>Biochemistry</i> , (1990), 29:2611-2617
	C28	Lohse, D., et al., <i>J. Biol. Chem.</i> , (1992), 267:24347-24355
	C29	Sasisekharan, R., et al., <i>Natl. Acad. Sci.</i> , (1993), 90:3660-3664
	C30	Sasisekharan, R., et al., <i>Proc. Natl. Acad. Sci.</i> , (1994), 91:1524-1528
	C31	Yang, V., et al., <i>J. Biol. Chem.</i> , (1985), 260:1849-1857
	C32	Kakkar, A., et al., "Venous Thromboembolism and Cancer", 1998, 675-687
	C33	Zucharski, L., et al., "Blood Coagulation Activation in Cancer: Challenges for Cancer Treatment", <i>Hamostaseologie</i> , 1995, 15:14-20
	C34	Alderman, C., et al., "Continuous Subcutaneous Heparin Infusion for Treatment ....", 1995, 29:710-713

EXAMINER

DATE CONSIDERED

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